	60132	S	TYROS? (S) HYDROX?
L3	5445	S	CMV AND PROMOTER
L4	110863	S	TETOP OR TETRACYCLINE OR "TET OPERON" OR (TETRACYLINE AND OPE
L5	3	S	L2 AND L3 AND L4
L6	3		DUP REM L5 (0 DUPLICATES REMOVED)
L7	567	S	L4 AND ADENOVIR?
L8	21	S	L7 AND L2
L9	10		DUP REM L8 (11 DUPLICATES REMOVED)
L10	0	S	"UPSTREAM MURINE SEQUENCE"
L11	13	S	"UPSTREAM MOUSE SEQUENCE"
L12	4		DUP REM L11 (9 DUPLICATES REMOVED)
L13	29525	S	PHOSPHOGLYCERATE KINASE OR DIHYDROFOLATE REDUCTASE OR ELONGAT
L14	3	S	L2 AND L13 AND L4
L15	58	S	L13 AND L2
L16	27		DUP REM L15 (31 DUPLICATES REMOVED)
L17	16	S	L16 NOT PY>=2000
L18	15235	S	TERMINATOR
L19	1	S	L2 AND L4 AND L18
L20	340	S	UMS
L21	0	S	L2 AND L4 AND L20
L22	0	S	L20 AND L4
L23	0	S	L20 AND L3
L24	0	S	L20 AND ADENOVIR?

NSWER 4 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:168217 CAPLUS
DOCUMENT NUMBER: 139:30244
TITLE: Regulated, **adenovirus**-mediated delivery of **tyrosine hydroxylase** suppresses growth of estrogen-induced pituitary prolactinomas. [Erratum to document cited in CA137:15411]
AUTHOR(S): Williams, Judith C.; Stone, Daniel; Smith-Arica, Joseph R.; Morris, Ian D.; Lowenstein, Pedro R.; Castro, Maria G.
CORPORATE SOURCE: Molecular Medicine and Gene Therapy Unit, School of Medicine, University of Manchester, Manchester, M13 9PT, UK
SOURCE: Molecular Therapy (2002), 5(2), 211
CODEN: MTOHCK; ISSN: 1525-0016
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The column headings in Table 1 were incorrect as printed; the corrected table is given.

L9 ANSWER 5 OF 10 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001692520 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11735344
TITLE: Regulated, **adenovirus**-mediated delivery of **tyrosine hydroxylase** suppresses growth of estrogen-induced pituitary prolactinomas.
COMMENT: Erratum in: Mol Ther 2002 Feb;5(2):211
AUTHOR: Williams J C; Stone D; Smith-Arica J R; Morris I D; Lowenstein P R; Castro M G
CORPORATE SOURCE: Molecular Medicine and Gene Therapy Unit, School of Medicine, University of Manchester, Room 1.302, Stopford Building, Oxford Road, Manchester M13 9PT, UK.
SOURCE: Molecular therapy : journal of the American Society of Gene Therapy, ((2001 Dec) 4 (6) 593-602.
Journal code: 100890581. ISSN: 1525-0016.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20011213
Last Updated on STN: 20020926
Entered Medline: 20020206
AB Prolactin-secreting adenomas are one of the most common types of intracranial neoplasm found in humans. The modalities of clinical treatment currently in use include D(2)-dopamine receptor agonists, surgery, and radiotherapy, and the success rates for treatment are good. However, there are prolactinomas that are difficult to treat. As an alternative, we have developed a gene therapy strategy in which the rate-limiting enzyme in dopamine synthesis, **tyrosine hydroxylase** (TH), is overexpressed in the anterior pituitary (AP) gland. Because dopamine is known to have an inhibitory effect on lactotroph growth and prolactin secretion, we developed a system that would enable its local synthesis from freely available precursor amino acids. A dual **adenovirus tetracycline**-regulatable expression system was generated to control the production of TH. In the absence but not presence of the **tetracycline** analog doxycycline, TH expression was observed in AP tumor cell lines AtT20, GH3, and MMQ. In both primary AP cell cultures and the AP gland, in situ expression of TH was seen in lactotrophs, somatotrophs, corticotrophs, thyrotrophs, and gonadotrophs in the absence but not presence of doxycycline. The ability of this system to inhibit hyperprolactinemia and pituitary lactotroph

hyperplasia was then assessed in a model of estrogen- or estrogen/sulpiride-induced pituitary tumors. In the absence but not presence of doxycycline, a 49% reduction in pituitary growth and 58% reduction in the increase of circulating prolactin levels were observed in estrogen, but not estrogen/sulpiride, treated rats. These results indicate that in situ dopamine enhancement gene therapy can be a useful tool for the treatment of prolactinoma. Dopamine synthesis can be tightly regulated and the therapeutic benefit of the system is only inhibited when local dopamine signaling is impaired.

L9 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:457223 CAPLUS
DOCUMENT NUMBER: 133:85129
TITLE: Method for improving transduction efficiency of adeno-associated virus 2 (AAV) by using human fibroblast growth factor receptor 1(FGFR1) as a co-receptor
INVENTOR(S): Srivastava, Arun; Qing, Keyun; Mah, Cathryn; Hansen, Jonathan; Zhou, Shangzhen; Dwarki, Varavani
PATENT ASSIGNEE(S): Advanced Research and Technology Institute, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039311	A1	20000706	WO 1999-US31220	19991229
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2358094	AA	20000706	CA 1999-2358094	19991229
EP 1141339	A1	20011010	EP 1999-968572	19991229
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002533128	T2	20021008	JP 2000-591202	19991229

PRIORITY APPLN. INFO.: US 1998-114596P P 19981231
WO 1999-US31220 W 19991229

AB The present invention provides a method for improving transduction efficiency of adeno-associated virus (AAV) by increasing gene expression of human fibroblast growth factor receptor (FGFR) and heparan sulfate proteoglycan (HSPG), and inhibiting single strand D-sequence-binding protein (ssD-BP) functions. The present invention relates to constructing a transgene expression cassette encoding FGFR or HSPG or both, wherein expression of FGFR and HSPG results in increased AAV infection. The invention also relates to inhibiting ssD-BP functions by manipulating phosphorylation states or reducing gene expression of ssD-BP. Also disclosed are methods for decreasing phosphorylated ssD-BP by reducing activities or gene expression of epidermal growth factor receptor (EGFR) tyrosine kinase. The invention further relates to the uses of methods of this invention in gene therapy.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:335583 CAPLUS

DOCUMENT NUMBER: 133:1452
TITLE: Control of transgene expression in nerve cells using **tetracycline**-responsive transactivator tTA
INVENTOR(S): Mallet, Jacques; Corti, Olga
PATENT ASSIGNEE(S): Aventis Pharma S.A., Fr.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000028062	A1	20000518	WO 1999-FR2752	19991109
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2786198	A1	20000526	FR 1998-14080	19981109
FR 2786198	B1	20030214		
EP 1129204	A1	20010905	EP 1999-971861	19991109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002529099	T2	20020910	JP 2000-581228	19991109

PRIORITY APPLN. INFO.: FR 1998-14080 A 19981109
US 1999-122600P P 19990303
WO 1999-FR2752 W 19991109

AB The invention concerns novel compns. and methods for controlling nucleic acid expression in cells. More particularly, it concerns any nucleic acid characterized in that it comprises: (a) a first region comprising a nucleic acid coding for a **tetracycline** (tTA)-dependent transactivator under the control of a moderate promoter; and (b) a second region comprising a nucleic acid of interest under the control of tTA sensitive promoter. The invention is more particularly useful for controlling the expression of transgenes in nerve cells, in vitro as well as in vivo, for example the gene for human **tyrosine hydroxylase**. Doxycycline-controlled expression of the human **tyrosine hydroxylase** cDNA in neurons was demonstrated. The cells were infected with an **adenoviral** vector containing the tTA gene controlled by the phosphoglycerate kinase promoter and a mouse c-mos gene-associated transcriptional terminator and the hydroxylase gene fused to the CMV promoter.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 10 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999449818 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10518586
TITLE: Long-term doxycycline-controlled expression of human **tyrosine hydroxylase** after direct **adenovirus**-mediated gene transfer to a rat model of Parkinson's disease.
AUTHOR: Corti O; Sanchez-Capelo A; Colin P; Hanoun N; Hamon M; Mallet J
CORPORATE SOURCE: Laboratoire de Genetique Moleculaire de la Neurotransmission et des Processus Neurodegeneratifs, Centre National de la Recherche Scientifique, UMR9923, Paris, France.
SOURCE: Proceedings of the National Academy of Sciences of the

United States of America, (1999 Oct 12) 96 (21) 12120-5.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199911
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991124

AB Developments of technologies for delivery of foreign genes to the central nervous system are opening the field to promising treatments for human neurodegenerative diseases. Gene delivery vectors need to fulfill several criteria of efficacy and safety before being applied to humans. The ability to drive expression of a therapeutic gene in an adequate number of cells, to maintain long-term expression, and to allow exogenous control over the transgene product are essential requirements for clinical application. We describe the use of an **adenovirus** vector encoding human **tyrosine hydroxylase** (TH) 1 under the negative control of the **tetracycline**-sensitive gene regulatory system for direct injection into the dopamine-depleted striatum of a rat model of Parkinson's disease. This vector mediated synthesis of TH in numerous striatal cells and transgene expression was observed in a large proportion of them for at least 17 weeks. Furthermore, doxycyline, a **tetracycline** analog, allowed efficient and reversible control of transgene expression. Thus, the insertion of a **tetracycline** -sensitive regulatory cassette into a single **adenovirus** vector provides a promising system for the development of successful and safe therapies for human neurological diseases. Our results also confirm that future effective gene replacement approaches to Parkinson's disease will have to consider the concomitant transfer of TH and GTP-cyclohydrolase transgenes because the synthesis of the TH cofactor tetrahydrobiopterin may be crucial for restoration of the dopaminergic deficit.

L9 ANSWER 9 OF 10 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999224289 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10207882
TITLE: A single **adenovirus** vector mediates doxycycline-controlled expression of **tyrosine hydroxylase** in brain grafts of human neural progenitors.
AUTHOR: Corti O; Sabate O; Horellou P; Colin P; Dumas S; Buchet D; Buc-Caron M H; Mallet J
CORPORATE SOURCE: Laboratoire de Genetique Moleculaire de la Neurotransmission et des Processus Neurodegeneratifs, C.N.R.S., Hopital de la Pitie Salpetriere, Paris, France.
SOURCE: Nature biotechnology, (1999 Apr) 17 (4) 349-54.
Journal code: 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990727
Last Updated on STN: 19990727
Entered Medline: 19990715

AB Ex vivo gene transfer is emerging as a promising therapeutic approach to human neurodegenerative diseases. By combining efficient methodologies for cell amplification and gene delivery, large numbers of cells can be generated with the capacity to synthesize therapeutic molecules. These cells can then be transplanted into the degenerating central nervous system (CNS). Applying this approach to human diseases will require the development of suitable cellular vehicles, as well as safe gene delivery

systems capable of tightly controlled transgene expression. For such brain repair technologies, human neural progenitors may be extremely valuable, because of their human CNS origin and developmental potential. We have used these cells to develop a system for the regulated expression of a gene of therapeutic potential. We report the construction of a single **adenovirus** encoding human **tyrosine hydroxylase** 1 (hTH-1) under the negative control of the **tetracycline**-based gene regulatory system. Human neural progenitors infected with this vector produced large amounts of hTH-1. Most importantly, doxycycline allowed a reversible switch of transgene transcription both in vitro and in vivo. This system may be applied to the development of therapies for human neurodegenerative diseases.

L9 ANSWER 10 OF 10 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 1999145149 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10022551
TITLE: Toward autologous ex vivo gene therapy for the central nervous system with human adult astrocytes.
AUTHOR: Ridet J L; Corti O; Pencalet P; Hanoun N; Hamon M; Philippon J; Mallet J
CORPORATE SOURCE: LGN, CNRS UMR 9923, Hopital Pitie-Salpetriere, Paris, France.
SOURCE: Human gene therapy (1999 Jan 20) 10 (2) 271-80. Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990413

AB The combination of gene transfer techniques and cell transplantation is a promising approach to deliver therapeutic molecules into the CNS. To optimize gene transfer systems, several neural and nonneural cell types are currently under investigation. Among these cells, astrocytes are particularly well suited because of their CNS origin, their efficient secretory mechanisms, and their role as neuronal support. Most importantly, the use of human adult astrocytes as cellular vehicles for ex vivo gene transfer may open the way to autologous transplantation, thus obviating immunological rejection and the side effects of immunosuppressors. In the present study, we report the ability of these cells to be expanded and genetically modified in vitro. Astrocytes derived from human adult cerebral cortex were grown and maintained in vitro as pure primary cultures for at least 10 months. In addition, cells were efficiently transduced by an **adenoviral** vector encoding human **tyrosine hydroxylase** (hTH) under the negative control of the **tetracycline**-based regulatory system (tet-off). The infected cells synthesized large amounts of active hTH and released L-dopa. In addition, doxycycline, a potent analog of **tetracycline**, efficiently regulated transgene expression. This work is a first step toward the development of therapeutic strategies based on the use of genetically engineered human adult astrocytes for autologous transplantation in human neurodegenerative diseases and CNS trauma.

ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1993:140898 CAPLUS

DOCUMENT NUMBER: 118:140898

TITLE: A new luciferase promoter insertion vector for the analysis of weak transcriptional activities

AUTHOR(S): De Martin, Rainer; Strasswimmer, John; Philipson, Lennart

CORPORATE SOURCE: Eur. Mol. Biol. Lab., Heidelberg, D-6900, Germany

SOURCE: Gene (1993), 124(1), 137-8
CODEN: GENED6; ISSN: 0378-1119

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A new luciferase-encoding expression vector , pUBT-luc, was generated by inserting the strong transcription termination signal from the mouse c-mos oncogene upstream from a multiple cloning site. This construct significantly reduced background transcription in NIH3T3 cells and has proven useful in the study of a weak promoter from the murine growth-arrest-specific gene gas-1.

ITLE: Activation of c-mos oncogene by integration of an endogenous long terminal repeat element during transfection of genomic DNA from mouse skin tumor cells.

AUTHOR: Wang S; Nishigori C; Miyakoshi J; Tsukada T; Shung B; Yagi T; Takebe H

CORPORATE SOURCE: Department of Experimental Radiology, Faculty of Medicine, Kyoto University, Japan.

SOURCE: Oncogene, (1993 Apr) 8 (4) 1009-16.
Journal code: 8711562. ISSN: 0950-9232.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 19930507
Last Updated on STN: 19930507
Entered Medline: 19930420

AB An activated c-mos oncogene was identified in a transformed clone of golden hamster embryo cells transfected with DNA extracted from cells cultured from a UV-induced mouse skin tumor. Southern blot hybridization with a v-mos oncogene probe showed that the mos oncogene was amplified in the primary and secondary transformed cells but not in the original tumor cells. Expression of the mos oncogene was very high in the primary and secondary transformants, but mos mRNA was undetectable in the original tumor cells. A genomic DNA fragment containing the activated mos oncogene was cloned and sequenced. The **upstream mouse sequence** of the mos oncogene, which functions as the transcription terminator, was lost and replaced by a mouse endogenous long terminal repeat (LTR) element that provides the promoter sequence, resulting in high expression of the gene. The rearrangement apparently occurred during transfection, since the polymerase chain reaction (PCR) product encompassing the junction region was present in the primary and secondary transformants but not in the original tumor cells. The LTR element is likely to have been amplified during the skin tumor development caused by UV irradiation. Southern blot hybridization showed that the copy number of LTR in the tumor cells was significantly higher than that in norma